

David A. Hafler, M.D.



Dr. Hafler is a physician-scientist whose investigations have significantly contributed to our understanding of human autoimmune disease with a particular emphasis on pathogenesis of multiple sclerosis (MS). In the 1990's he identified T cell targets of the myelin antigens underlying the disease defining the structural basis of T cell receptor recognition of these self-antigens. He identified human FoxP3 regulatory T cells and was the first to report a defect in their function in common human autoimmune diseases. He cofounded the establishment of the International MS Genetics Consortium that has identified over 100 allelic variants that define disease risk and recently identified a possible environmental cause of autoimmune disease. Dr. Hafler is the Gilbert H. Glaser Professor of Neurology and Immunobiology and Chairman of the Department of Neurology at the Yale School of Medicine, New Haven, CT.

Training

He graduated magna cum laude from Emory University with combined B.S. and M.Sc. degrees in biochemistry, and then Alpha Omega Alpha (AOA) from

the University of Miami School of Medicine. He completed his internship in internal medicine at Johns Hopkins followed by a neurology residency at Cornell Medical Center-New York Hospital in New York. Dr. Hafler received training in immunology at the Rockefeller University and then at Harvard where he joined the faculty in 1984. He did a sabbatical at the Whitehead Institute in 2000.

Research Accomplishments

Dr. Hafler is world renowned for his research in the field of MS and autoimmunity. His work has advanced the knowledge of how pathogenic T cells recognize self-antigens, and how these T cells are dysregulated. He was a major force in establishing the international consortium that led to the establishment of the International MS Genetics Consortium that identified the genetic variants that cause MS. His recent work has identified possible environmental factors critical for the disease pathogenesis.

Dr. Hafler's early work defined immunodominant epitopes of myelin antigens, developing new technologies to measure both functionality and frequency of autoreactive T cells¹. These studies clearly demonstrated that autoreactive T cells are present in the circulation both of patients with autoimmune disease and healthy individuals, but that in patients the autoreactive T cells are activated². He described how these self-antigens bind MHC and are recognized by T cell receptors. The Ob1A12 T cell receptor from his laboratory is the most investigated human T cell receptor recognizing an autoantigen and was the first to be crystalized. With his collaborators he was the first to experimentally use monoclonal antibodies to treat human autoimmune disease³.

He investigated the functional defects of immune regulation in patients with MS. CD4⁺FoxP3⁺ regulatory cells had been identified in mice, but it was not clear that they were important in humans. Dr. Hafler was among the first to identify these regulatory cells in humans⁴ and then went on to show that they are dysfunctional in human autoimmune disease⁵. He has recently identified the possible mechanism for this loss of immune regulation demonstrating the regulatory T cells in patients with MS secrete inflammatory cytokines preventing their functionality⁶. Besides his work in autoimmunity, Dr. Hafler has made seminal contributions to understanding the human immune system function⁷.

More recently, Dr. Hafler has focused on broadly characterizing the molecular pathogenesis of the disease, both at the DNA, mRNA, and proteomic level. Dr. Hafler is a co-founder of the International MS Genetic Consortium, a group formed to define the genetic causes of MS including. His seminal paper in the New England Journal of Medicine⁸ was the first to identify the genes causing MS. The work of the Consortium has continued with over 80 original publications, culminating in a recent publication in Nature clearly demonstrating the MS is an immune mediated disease clustering with other autoimmune diseases⁹. This work continues as he has intensively investigated the biologic function of these genetic variants¹⁰.

Dr. Hafler's most recent work identified a common environmental factor, salt, induces the activation of inflammatory cells with the induction of IL-17 and GM-CSF secretion. Feeding mice a high salt diet leading to disease worsening¹¹. These findings suggest a potential role of dietary factors in the causality of human autoimmune diseases.

Leadership Positions

Dr. Hafler is Chairman of the Yale Department of Neurology. He is Founder of the Federation of Clinical Immunology Societies, the leading international society for the investigation of inflammatory human diseases. He has been on numerous executive committees including the NIH's Immune Tolerance Network, International Society of Neuroimmunology, Executive Council; Vth International Congress Immunology, Co-Organizer; NIH Neuroscience Blueprint Committee; NIH Biomarkers Consortium Inflammation & Immunity Steering Committee; Steering Committees: NIH U19 Autoimmunity Prevention Center; Autoimmunity Centers of Excellence, U19 Human Vaccine Grant. He is on the editorial board of the Journal of Clinical Investigation and the Journal of Experimental Medicine.

Awards

Dr. Hafler has received numerous awards and honor for his work including the NIH The Javits Neuroscience Investigator Award, selection as a Harry Weaver Scholar of the National Multiple Sclerosis Society, election into American Society for Clinical Investigation, Honorary Membership in the Scandinavian Society for Immunology, ISI Most Highly Cited List, and the University of Miami "Annual Distinguished Alumni Award". In 2010 he received the John Dystel Prize for Multiple Sclerosis Research by the American Academy of Neurology

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